

**REMARKS**

**Preliminary Matters**

Applicants respectfully request that the Examiner consider the IDS filed on September 30, 2008 and return a signed copy of the SB/08 Form, indicating that these documents have been considered.

**Rejection under 35 U.S.C. § 103(a)**

Starting on page 2 of the Office Action, claims 1-19 are rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Tsugita et al (Electrophoresis, 1998) (“Tsugita”) in view of Tsugita et al. ‘1992 (Chemistry Letters, 1992) (“Tsugita ‘1992”’) and Covey et al (US Patent No. 5,952,653) (“Covey”). Applicants presume the rejection is also based on Vogt et al. as well (Polymer Bulletin, 1996) (“Vogt”), because the Examiner’s explanation of the § 103 rejection explicitly includes Vogt on page 7, fourth full paragraph.

Applicants respectfully submit that the presently claimed invention is not rendered obvious by the cited references for at least the following reasons.

**Claim 1 Requires Vapor Phase Reactants**

First, claim 1 recites “pretreatment step . . . of allowing an alkanoic acid anhydride and an alkanoic acid both of vapor phase . . . to act on a dry sample. . . .” Tsugita does not appear to teach this requirement of claim 1.

In contrast, Tsugita teaches the treatment of samples with acetic anhydride with 20% acetic acid in tetrahydrofuran. See page 930, column 2, third paragraph of the Office Action. Therefore, Applicants respectfully submit that Tsugita does not teach the requirement of claim 1

for alkanoic acid anhydride and alkanoic acid in the vapor phase, because Tsugita specifically calls for this reaction to be performed in solution.

In addition, claim 1 also requires “a step of allowing an alkanoic acid anhydride and a perfluoroalkanoic acid both of vapor phase . . . to act on the dry peptide sample. . . at a temperature selected in a range of 15°C to 60°C” and “a post-treatment of removing the remaining alkanoic acid anhydride and perfluoroalkanoic acid in a dry state, and then supplying vapor of a basic nitrogen-containing aromatic compound or a tertiary amine compound and water molecules, all of vapor phase . . .” In contrast, Tsugita merely teaches treatment with a 5% solution of perfluoropropionic methyl ester (PFPM<sub>e</sub>) in methanol and dimethylamino ethanol (DMAE) in a water solution, respectively.

Therefore, Tsugita does not render obvious claim 1, because Tsugita does not teach all the requirements of claim 1.

Moreover, Applicants respectfully submit that Tsugita cannot properly be combined with the teachings of Tsugita ‘1992, because there is no sufficient teaching, suggestion, motivation, or other reason to combine Tsugita with Tsugita ‘1992. Tsugita is directed to a solution phase method for selectively releasing N-terminal amino acids, where an acetic acid anhydride and acetic acid are applied to the sample in a tetrahydrofuran (THF) solution, then the result is run on a minicolumn; PFPM<sub>e</sub> is applied to the sample in methanol, then the result is subjected to a pulse-liquid reaction on a minicolumn; and dimethylamino ethanol (DMAE) is applied to the sample in water. See page 930, column 2, third paragraph of Tsugita. Therefore, Applicants assert that Tsugita cannot be modified by Tsugita ‘1992, because the reactions of Tsugita are deliberately designed to be performed and conducted in solutions for further processing on minicolumns, so to modify this aspect of Tsugita would render Tsugita impractical for Tsugita’s

purpose of subjecting the sample to minicolumns for further processing. Since Tsugita was written around six years after Tsugita '1992 and includes common authors, such as *Akira Tsugita* and *Keiji Takamoto*, and includes multiple examples of perfluoropropionic acid (PFPA) used in the vapor phase, it is fair to conclude that authors of Tsugita were aware of the vapor phase process performed in Tsugita '1992 when the authors of Tsugita chose not to use them for performing the cited method of Tsugita.

Applicants also note that Tsugita cites multiple procedures for exposing samples to the vapor of PFPA at 90°C, yet these procedures do not appear to involve the pretreatment method of using an alkanoic acid and a alkanoic acid anhydride. See, for example, the captions for Figures 1, 2, and 4 of Tsugita. Therefore, it seems clear that Tsugita intentionally chose to use PFPM<sub>e</sub> in the solution phase for the cited procedure in direct contrast to Tsugita's other procedures.

Vogt and Covey do not appear to remedy this deficiency.

Claims 2-11 depend from claim 1.

For at least the above reasons, the proposed combination of Tsugita, Tsugita '1992, and the other cited references does not render claims 1-12 obvious.

**There Is No Sufficient Motivation to Combine Tsugita and Tsugita '1992, Because PFPA and PFPM<sub>e</sub> Are Not Fungible**

Applicants respectfully submit that the presently claimed invention is not rendered obvious by the cited references, because there is no sufficient teaching, suggestion, motivation, or other reason to substitute the PFPA of Tsugita '1992 for the PFPM<sub>e</sub> in the method of Tsugita.

Claims 1 and 12 each require a step of allowing an alkanoic acid and a perfluoroalkanoic acid to react with the sample.

The Examiner asserts that PFPM<sub>e</sub> and PFPA have similar structures and functions, and it therefore would be obvious to use PFPA in the sub-step of Tsugita's procedure based on teachings of Tsugita '1992. See page 3, first paragraph, and page 6, last paragraph of the Office Action, respectively.

Applicants respectfully disagree. There is no sufficient teaching, suggestion, motivation, or reason to substitute the PFPA of Tsugita '1992 for the PFPM<sub>e</sub> of Tsugita. First, Applicants assert that one of ordinary skill in the art would immediately recognize a drastic difference in reactivity and structure between a carboxylic acid and an ester. This difference in reactivity appears to be appreciated by both Tsugita and Tsugita '1992, because Tsugita '1992 seems to employ the more acidic PFPA to a sample at a temperature of -18°C. In contrast, Tsugita only teaches the use of the reactive PFPM<sub>e</sub> at a temperature of 5°C in methanol. Therefore, Applicants submit that there is no proper motivation to substitute the more acidic of Tsugita '1992 being used at -18°C in vapor for the less acidic PFPM<sub>e</sub> of Tsugita at 5°C in methanol, to reach the claims 1 and 12, which both require a higher reaction temperature than either reference.

Vogt and Covey do not appear to remedy this deficiency.

Claims 2-11 and 13-19 depend from either claim 1 or 12.

For at least this reason, the presently claimed invention is not rendered obvious by the cited references.

**Tsugita Does Not Teach Maintaining Acetic Anhydride In the Cleavage Sub-Step**

Claims 1 and 12 each require both perfluoroalkanoic acid and alkanoic acid anhydride for the cleavage sub-step. The Examiner has conceded that Tsugita does not specifically teach “maintaining acetic anhydride in the cleavage sub-step.” See page 3, second paragraph of the Office Action. However, the Examiner has asserted that it would be obvious that maintaining the concentration of acetic anhydride in the cleavage sub-step may benefit the reaction.

Applicants respectfully disagree. Applicants assert that there is no teaching, suggestion, motivation, or other reason to maintain the presence of acetic anhydride in Tsugita, because, as stated by the Examiner, the function of acetic anhydride is to form oxazolone. See page 3, second paragraph of the Office Action. Tsugita teaches that “[t]he first reaction was acetylation of the N-Terminus and formation of an oxazolone at the C-terminal carboxyl group.” See page 930, column 2, paragraph 3 of Tsugita. Therefore, at the end of the first reaction, the oxazolone ring is already formed and acetic anhydride has already finished its only apparent function according to Tsugita and the Examiner. Thus, there does not seem to be any reason in Tsugita to maintain the presence of acetic anhydride in the cleavage step, nor has the Examiner stated why it might be considered beneficial to the cleavage reaction. Also, Applicants submit that it is highly unusual and unadvisable for one of ordinary skill in the art to add or maintain reactants from a previous reaction during a separate subsequent reaction without a specific reason for doing so, because such a careless practice only invites side reactions, contamination, and safety issues later in a chemical process.

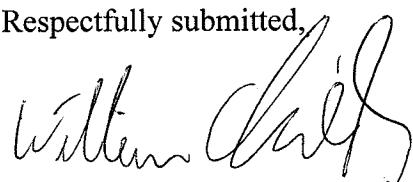
Neither the cited references, nor the general teaching in the art appear to suggest a reason or motivation to maintain the presence of acetic anhydride during the cleavage sub-step of Tsugita.

Therefore, Applicants respectfully submit that for at least this reason the presently claimed invention is not rendered obvious by the cited references.

In view of the above, reconsideration and allowance of this application are now believed to be in order, and such actions are hereby solicited. If any points remain in issue which the Examiner feels may be best resolved through a personal or telephone interview, the Examiner is kindly requested to contact the undersigned at the telephone number listed below.

The USPTO is directed and authorized to charge all required fees, except for the Issue Fee and the Publication Fee, to Deposit Account No. 19-4880. Please also credit any overpayments to said Deposit Account.

Respectfully submitted,



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